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In re Application of
Queen

Application Number	Filed
07/310252	2,13,89

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United States Patent [19]

Queen et al.

[11] Patent Number: 5,693,761

[45] Date of Patent: Dec. 2, 1997

[54] **POLYNUCLEOTIDES ENCODING IMPROVED HUMANIZED IMMUNOGLOBULINS**

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[73] Assignee: **Protein Design Labs, Inc.**, Mountain View, Calif.

[21] Appl. No.: **474,040**

[22] Filed: **Jun. 7, 1995**

Related U.S. Application Data

[62] Division of Ser. No. 634,278, Dec. 19, 1990, Pat. No. 5,530,101, which is a continuation of Ser. No. 590,274, Sep. 28, 1990, abandoned, and a continuation of Ser. No. 310,252, Feb. 13, 1989, abandoned, which is a continuation of Ser. No. 290,975, Dec. 28, 1988, abandoned.

[51] **Int. Cl.**^{6} **C07H 21/04**

[52] **U.S. Cl.** **536/23.53**; 530/387.3; 435/320.1; 435/252.3

[58] **Field of Search** 536/23.53; 530/387.3; 435/320.1, 252.3

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[57] **ABSTRACT**

Novel methods for producing, and compositions of, humanized immunoglobulins having one or more complementarity determining regions (CDR's) and possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the CDR's, amino acids from the donor immunoglobulin framework that are, e.g., capable of interacting with the CDR's to effect binding affinity, such as one or more amino acids which are immediately adjacent to a CDR in the donor immunoglobulin or those within about about 3 Å as predicted by molecular modeling. The heavy and light chains may each be designed by using any one or all of various position criteria. When combined into an intact antibody, the humanized immunoglobulins of the present invention will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such as a protein or other compound containing an epitope.

37 Claims, 55 Drawing Sheets